Alternative Cancer Therapies

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Smith Ridge Veterinary Center

Smith Ridge Veterinary Center is a three doctor, small animal hospital with a special emphasis on holistic medicine and the use of natural therapies to treat chronic degenerative diseases. The hospital is located on 400 Smith Ridge Road (Route 123) South Salem, New York 10590. Telephone(914) 533-6066. Fax (914) 533-6405.

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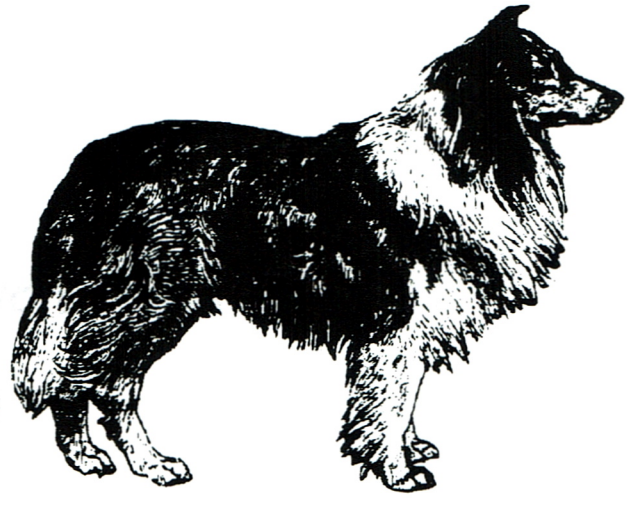

Alternative Cancer Therapies

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1. Cancer in dogs and cats

Cancer is the second most common cause of human deaths in the United States. Approximately one out of every three Americans will acquire some form of cancer during his or her lifetime. The situation is no better among our companion animals.

Cancer, kidney and heart disease are the leading causes of death in dogs and cats. In a recent survey sponsored by the Morris Animal Foundation, cancer was perceived as the number one health concern among 1,492 respondents who own dogs.[1] Cancer leads heart, kidney, and urinary tract disease as the number one killer of dogs, cats, pet ferrets, rabbits, and birds. Sadly, we see fewer pets dying simply of "old age". It is interesting to note that the estimated incidence of cancer is less than 2 percent in wild animals. Despite the popular notion that veterinary care "prevents" disease (through vaccinations, flea and heartworm medications), we are doing little to prevent cancer-related illness and death.

Top five disease-related deaths in companion animals.*

Dogs		**Cats**	
Cancer	47%	Cancer	32%
Heart disease	12%	Kidney/urinary tract disease	23%
Kidney disease	7%	Heart disease	9%
Epilepsy; Liver disease	4%	Diabetes	6%
Diabetes; Bloat	3%	FIP; FIV infection	5%

* Among survey respondents, disease was the leading cause of death (60%), followed by old age (31percent) and accidents (9 percent). Reported in: *Veterinary Product News*, June 1998. p. 11

Drastic methods are employed to fight cancer. For decades, dogs, cats and people have undergone exhausting, painful, and oftentimes disfiguring treatments with surgery, radiation or chemotherapy in an effort to stop the progression of this disease. New cases of

cancer have increased every decade of this century, and the medical costs to treat cancer have risen in step with the case load.

What causes cancer? And what alternative or complementary therapies are available that will prolong survival, reduce costs, and improve the quality of life in our patients? This seminar offers an up-to-date assessment of natural cancer therapies that have few adverse effects, promote healing, and support the body's immune system. Ultimately they may be less expensive to acquire and administer than conventional therapy, since most of the treatments can be provided to the patient at home.

Risk Factors

Cancer is uncommon among wild animals in their natural environment. We can safely say it is a disease of "modern living" where improper diet, unhealthy lifestyle, and exposure to toxins increases the likelihood of genetic mutations and expression of pro-cancer genes, or *oncogenes.*

Seemingly harmless modifications to food such as the use of preservatives to retard spoilage may contribute to an individual's risk of cancer. For example, studies have established a link between synthetic preservatives such as ethoxyquin, and butylated hydroxytoluene (BHT), with cancer.[2,3,4] Unfortunately, natural preservatives such as ascorbyl palmitate and mixed tocopherols may not be as effective as synthetic antioxidants in preserving pet food.[5]

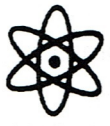
Fiber

The protective effects of dietary fiber in preventing certain forms of cancer is well established. Yet commercial pet food manufacturers seem to be promoting the exact opposite: a *low fiber* diet. Full-page advertisements in our veterinary journals promote one brand of dog food as having "84% total digestibility for improved stool quality".[6] The two leading brands of adult maintenance dog food contain less than 2 percent fiber, "for improved stool quality" or so we are told. No one seems to notice that pets and people both need

more fiber in their diet, not less. High levels of soluble and insoluble dietary fiber are associated with optimum fermentation in the colon, normal motility and smooth muscle tone, and a healthy population of microorganisms. Bacteria in the colon ferment dietary fiber, producing volatile fatty acids such as acetate, butyrate, and proprionate. These short-chain fatty acids have a protective effect against colon cancer, and provide a more sustained release of blood glucose from food. Much more will be said about the diet-cancer connection throughout the seminar.

Electronic pollution

Who would believe that television programming could affect our health? Individuals may feel nauseated from watching a violent scene on television or film, but the most astounding reaction came from 700 children with history of seizure disorders who fell ill after watching their favorite cartoon. The animated children's show, "Pocket Monsters" triggered mass *photo stimulation* among TV viewers in Japan, with hundreds of youngsters feeling dizzy or complaining of headaches, nausea, respiratory difficulty, or seizures after watching the program.



Flashing, brightly colored red light emitted at frequencies between 10 and 30 hertz can stimulate neural discharge and induce seizures. Medical experts are calling this phenomenon "optically stimulated epilepsy" which affects some 10,000 people in Japan. Children with a low seizure threshold are particularly sensitive to photostimulation and are at risk of having seizures from these broadcasts.[7] More research is needed to better understand the role of artificial lighting, electromagnetic fields, and other low-level energies on our health.

Carcinogens

The list of individual risk factors for cancer is as diverse as the genome itself, for the connection between damage to the genetic material, DNA and RNA, and neoplasia is well established. Avoidance of common carcinogens in the air, water or home may be unavoidable. What is important is reducing the *cumulative dose* of chemicals, lifestyle modifica-

tions, and dietary factors that promote carcinogenesis. Below is a short list of known risk factors or tumor promoters in humans. To this list we might add certain veterinary chemotherapy agents (cyclophosphamide), treatments (radiotherapy), vaccines (feline vaccine induced fibrosarcoma), pesticides, food preservatives (BHT, ethoxyquin), and low fiber commercial pet food. The current debate within our profession over risk-benefit of routine vaccinations is long overdue.[8,9,10,11]

Risk Factors	Source	Associated cancer in humans
Indoor air pollution	Second-hand tobacco smoke Radon gas Air fresheners	Lung, cervix, mammary, oral Lung Unknown
Benzene compounds, hydrocarbons	Paint and gasoline fumes	Lung, liver, esophagus, pancreas, kidney, bladder
Electromagnetic fields, radiation	Electrical appliances	Leukemia
Hazardous building materials	Asbestos; possibly glues, resins, insulating foams	Lung
Improper diet	Excess salt and saturated fat	Mammary, colon cancer
	Insufficient fiber and fresh foods	Mammary, colorectal, stomach, prostate
Obesity	Calorie-dense diets	Mammary, colon
Hormone therapy	Diethylstilbesterol (DES)	Mammary, vagina, cervix

Summary

Cancer is one of the leading causes of death in small animals. In humans, 80 to 90 percent of all cancers are related to nutritional factors, lifestyle, or exposure to toxic chemicals. There is little reason to believe that the dogs and cats that share our environment are any different. New cases of cancer can be reduced through early recognition of risk factors and client education. The goal of risk factor modification is to prevent cancer and aid in the early detection of this and other chronic, degenerative diseases.

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2. Physical exam

Patient history

Careful evaluation of the cancer patient is important for a successful outcome. Start by obtaining the patient's history. Ask the usual questions about bowel movements, urination, water consumption, vomiting, diarrhea, coughing, sneezing, and adverse drug effects. You also need to know: vaccination types and date administered, previous and current medications, diet and water supply.

The patient's history often provides some clues to the underlying problem. Pay attention to these early warning signs:

* chronic cough or hoarse voice
* halitosis (bad breath)
* a palpable mass with a sudden increase in size
* generalized or local lymphadenopathy
* abdominal pain
* weight loss
* chronic diarrhea
* hematuria

Neoplasia tends to develop along a progressive, insidious course. Previous radiographs, medical records, and diagnostic test results should be obtained to better understand the patient.

Systems approach

My approach to a physical exam differs little from what we learned at veterinary school. We take an organ system approach and evaluate the patient from nose to tail. The examination has been modified somewhat to include measures of the patient's acid-base balance, acupuncture meridians, and iridology. My findings are written in the medical record in the SOAP format.

S: subjective comments about the patient's mentation, appearance, and preferences.

O: objective findings covering the eyes, ears, nose, throat, cardiovascular, respiratory, genitourinary, gastrointestinal, musculoskeletal, integument, and neurologic systems.

A: assessment of the patient (including signalment) and presumptive diagnosis or differential diagnoses.

P: treatment and diagnostic plan. Rule in, rule out certain diseases. Prioritize the treatments. Suggest follow-up dates and further diagnostic tests.

The patient history, diet, and chief complaint(s) are also recorded in the record. I frequently include stickers with the canine or feline dental formula, or line drawings to illustrate the location of masses, skin lesions, and areas of hair loss.

pH

A small strip of pH color test paper is very useful for measuring the pH of the patient's saliva. These pH-test paper strips can also be used to measure the acid or alkaline status of vaginal secretions, urine, or feces. Approximately ninety-five percent of the dogs that I have tested had an oral pH around 8 on presentation. It is interesting that approximately the same percentage of owners had a neutral pH of their saliva.

Physical examination

I record the patient's body condition score on a scale of 1 (emaciated) to 5 (obese). This helps to identify potential drug dosage modification given the smaller volume of distribution of a thin, geriatric patient compared to an obese, middle age patient. Comments on muscle tone, muscle mass, and posture (lordosis, kyphosis, scoliosis, etc.) will also be entered if appropriate for the case.

Using a rubber-tipped neurology hammer I gently thump over the dorsal spinous processes, looking for increased sensitivity over the vertebrae and intervertebral disks. In female dogs I examine the vaginal mucosa for viral or yeast plaques, erythema, or discharge. Male dogs need to have a digital exam per rectum to evaluate the prostate and anal glands. Dogs with a history of colitis or hematochezia (frank blood in the stool) also should have their distal colon and rectum palpated.

Iridology

I routinely observe and comment on changes to the iris. The study of iridology goes back 150 years to Ignatz von Peczely, a physician in Hungary who made the association between degenerative changes in an organ or anatomic area and a specific location of the iris.

The iris is densely innervated by the sympathetic and parasympathetic nervous system. Under stressful conditions we know the iris will contract, dilating the pupil. When a chronic, degenerative process is going on in an organ, these nerves are under constant stimulation (or irritation). These changes are manifested in the iris, which also deteriorates at specific locations. The more severe the stressor, the greater the degree of iris degeneration. At one extreme is the removal of an organ, say a nephrectomy, that causes the iris region corresponding to the ipsilateral (missing) kidney to be "blacked out", or completely degenerate. When a stress or disability resolves, the iris has the capacity for repair though some changes (e.g., removal of an organ) may result in permanent iris lesions.

The most common abnormality I see is a dark, peri-pupillary rim of the irides. This location corresponds to the stomach and intestines. Consistently these are dogs on commercial pet food and nothing else. Dogs that receive topical once-a-month flea adulticides (or other lipophilic toxins) often have a dark iris periphery; this region corresponds to the skin and lymphatics. Puppies and older, healthy dogs on "people-quality" diets rarely, if ever, exhibit these changes. Pets with severe organ disease such as hepatitis, chronic nephritis, or heart disease show iris deterioration at specific regions, conveniently mapped out on iridology charts. The chart I use is produced by Dr. Bernard Jensen, a chiropracter who did much to define and popularize iridology in this country. Iridology, while not diagnostic, is a simple process that provides a fascinating "window" to the body's organs.

Client education

After discussing the physical exam findings with the client, I discuss the steps and estimated cost to obtain a diagnosis. This may include the expense of laboratory tests, diagnostic imaging, biopsies, urinalysis, or consultation with specialists, as necessary. Cancer is an expensive disease to treat. Make every effort to be sure you know the type of cancer, histological stage or grade, and extent in each patient.

3. Natural food for pets

I am a second generation doctor. My father is a physician in internal medicine and has been in private practice for 42 years. His practice occupied the ground floor of our house and my parents worked together running the office and raising five children. Providing service to patients was second nature to my family, and I think it has made me a better veterinarian for having that experience. More important to this topic of "natural food for pets" was my parents interest in nutrition and the smooth integration of natural therapies into their medical practice.

Many terms have been used to describe it, but basically a good doctor helps to educate patients so they can take care of themselves. The best form of medical care emphasizes *prevention* of disease rather than the more prevalent view of *intervention* that is so rampant in human and veterinary medicine today. At Smith Ridge Veterinary Center, we emphasize natural therapies to treat disease in small animals. Most of our case load involves treatment of a wide range of chronic, degenerative diseases and non-toxic cancer therapy. We rely almost exclusively on nutritional supplements, Chinese and Western herbs, homeopathic remedies, glandular extracts, acupuncture, and other natural approaches to treat disease and promote healing.

During this seminar I want to share with you our experiences in treating cancer, but more important to lay the groundwork for prevention and treatment of all the common health problems we see in dogs and cats. But first, I'd like to ask: *What are the three most common health disorders of middle age cats and dogs?*

And what would you do about it?

Poor nutrition

The three most common health disorders I see all relate to poor nutrition. They are:

1. **A total lack of fresh food, especially vegetables**
2. **Incomplete fat metabolism, with oxidative stress**
3. **Mineral imbalance (high sodium, low magnesium, etc.)**

All animals need fresh food! There isn't an animal on the planet that doesn't require fresh food in their diet. One of the two biggest falacies in pet nutrition is to believe that cats and dogs are just meat eaters. The other holds that all good quality commercial pet foods provide "complete and balanced nutrition".

Varied diets

First, dogs are omnivores. They have a digestive system very similar to our own and require a variety of foods to be healthy. The wild dog doesn't just pick off muscle tissue (meat) off the carcass, but consumes the organs, and all the plant material that the small mouse, rabbit, or duckling ingested. The wild canid is consuming berries and leafy plants as well. These fresh plant foods are extremely important to our animal's good health.

The trend among pet food manufacturers is to promote "high digestibility" of their products, leaving a *small, firm* stool. Nothing could be worse for the dog! Dogs need some complex carbohydrates that are fermented by bacteria in the colon and produce volatile fatty acids such as proprionate, butyrate, and acetate. These volatile fatty acids are converted into glucose that provides energy for the intestinal mucosa, and have anti-cancer properties.

Dry foods

In order to manufacture a kibble of dry food, basic ingredients such as corn, wheat by-products or rice are milled into very fine feed particles. These fines get broken down rapidly in the stomach and small intestine, causing a rapid rise in blood sugar and insulin de-

mand. But they leave little for bacteria at the distal end of the gastrointestinal tract to live on. The result is a food that gives a short burst of energy for the dog but leaves him unsatisfied a few hours later, and they will go back for more food. Our interpretation of this is "the dog likes the food". My interpretation is the dog is hungry again and low blood glucose drives his appetite center in the brain to seek more food.

Many pet owners make routine trips to the groomer or veterinarian to have the pet's anal glands expressed. These scent glands (located at 4:00 and 8:00 around the rectum) are squeezed every time the cat or dog has a normal bowel movement. If there is inadequate fiber in the diet, the anal glands can become full or impacted. With chronic impaction the glands can become inflammed, then infected, and finally can become dysplastic. The end stage of chronically irritated tissue is rampant proliferation of cells, i.e., cancer. Constipation, colitis, and impacted anal glands are diseases of modern living and poor nutrition. These conditions can be entirely prevented by providing adequate levels of fiber and fresh foods in the diet.

Deficiencies

Many middle aged pets have sore, inflamed gums and rotten teeth. These animals are *scorbutic*. Like old sailors out at sea they have too little fresh food and insufficient vitamin C to maintain the body's natural wear and tear mechanism. Dogs and cats can synthesize some vitamin C from amino acids in their liver, about 40 mg a day. But that amount of ascorbic acid is not enough to meet their needs, especially during times of stress, illness, or toxic load.

What are some toxins that would raise the daily requirement for vitamin C? Medications of all types, monthly flea control products, heartworm preventatives, second hand cigarette smoke, electromagnetic and microwave radiation, excess ultraviolet light, xenobiotics (ingested toxins), rancid fats, trans fatty acids (animal and vegetable fats), food dyes, preservatives, lawn pesticides, heavy metals in our drinking water, and many others.

Feeding fresh food to pets doesn't have to be difficult. I've prepared a handout to help you. I tell my clients that they don't have to be religious about cooking for their pet, but every pet needs some vegetables, fruit, and complex carbohydrates in order to avoid expensive health care later in life.

The answer to poor animal nutrition is not a long list of supplements added to a bag or can of pet food. It's the change to a varied diet of fresh, whole foods that will keep pets truly healthy. Many young animals develop a habit of begging at the table. We punish them for communicating to us that their food looks, smells, and tastes bad. Is it any wonder that they want a share of our meal?

I don't advocate feeding pets the same thing that you are eating for dinner. I do recommend feeding pets their own food, but it is made from ingredients that would be good enough for you to eat. In our practice we recommend simmering a pot of stew once a week, freezing most of it to feed your pet for a week or two.

It is very easy to prepare a big batch of stew for a cat or small dog, freeze it in small dinner-size containers, and give your pet nutritious food. The ingredients do not have to be expensive. You can use inexpensive ingredients like carrots, potatoes, oatmeal, rice, broccoli, eggs, and inexpensive cuts of meat. The stew can be as simple or elaborate as you want, as long as you use fresh ingredients.

> ***Remember, all dogs and cats need fresh food. They cannot be healthy eating out of a can or bag their entire life, any more than we can.***

We've all been led to believe that the only know-how in pet nutrition is from pet food manufacturers. Nothing could be farther from the truth! They are in the business of turning low quality ingredients— *byproducts,* into value-added products, through clever market-

ing. If you feed yourself a healthy, balanced diet, you can feed your cat or dog a good diet. It's not that difficult.

If you need the convenience of pet food, go ahead and buy it. But at least offer some fresh foods on the side to compensate for what is a highly processed and artificial product.

Snacks

Fresh foods can be given to cats or dogs every day as snacks. Some of my favorite snacks for dogs include frozen berries and green vegetables: blueberries, blackberries, lima beans, Brussels sprouts and green beans. These are wonderful snacks for dogs, low in calories, low fat, and inexpensive.

Cats like sprouted grains, such as those made from wheat, barley, or oats. It is amazing what pets will eat when their palate has been enlightened. Feeding our pets appropriately would go a long way towards eliminating early onset diabetes, arthritis, cataracts, periodontal disease, kidney, liver and heart disease, allergies, and seizure. The list is endless.

Sodium

Ninety-five percent of the dogs I see have an oral pH of 8— too alkaline. They have so much sodium (or too little potassium and magnesium) that the body has difficulty eliminating it. Fifty percent of the dogs I see have low serum magnesium levels. These electrolyte or mineral imbalances are affecting cardiovascular health and many other physiologic functions.

Pet food manufacturers are not required to disclose the sodium content of the foods on the product label, though it probably varies widely among different foods. Water as a source of sodium should not be overlooked, especially in the Western States. Some pets receive too much sodium by drinking tap water that has passed through a water softener. Your local health officer can direct you to certified water testing laboratories for dissolved mineral analyses.

We treat dogs that have salt imbalance with other minerals, vitamins A and C, and freeze-dried raw adrenal gland supplements. The adrenal glands produce the hormone *aldosterone* which acts on receptors in the renal tubules to conserve sodium and eliminate potassium. Supporting adrenal gland function (or pancreas, thyroid, thymus, etc.) with nutritional gland supplements (*glandulars)* can help the body regain balance without harmful side effects.

Magnesium

Dogs with low magnesium can receive diet supplements, or we could feed more green foods. The green plant pigment *chlorophyll* is a chelate of magnesium, whereas meat, fish, and dairy products are relatively poor sources of this mineral. Magnesium is a very important macromineral. It is part of over 200 different enzymes; helps regulate heart rhythm; has natural antihistamine properties; and raises the threshold for pain, something very important in arthritis patients. Magnesium acts as a natural bronchodilator and is one of my first line treatments for asthma. For patients with excess sodium, dietary modification with potassium and magnesium can help resolve long standing imbalances.

Obesity

Veterinarians see a lot of overweight dogs and cats. I'm not biased against these pets or their owners. Obesity is largely a problem of client education, but stems from our near total reliance on commercial pet foods in the last fifty years.

Fat mobilization, metabolism, and excretion involves the activity of the liver, stomach, pancreas, gall bladder, adrenal glands, nervous system, reproductive organs, lungs, and so on. Decreasing calories in the diet oversimplifies the steps needed for a dog or person to lose weight. Actually, many obese dogs would benefit from a high protein, low carbohydrate diet. They may need supplements of lecithin, magnesium, B-vitamins, lipotropic factors, or digestive enzymes to facilitate the turnover or oxidation of body fat.

We help overweight dogs by prescribing specific supplements to help them emulsify fats, improve liver function, and excrete excess cholesterol and fatty acids in bile. I commonly prescribe calcium and/or magnesium (involved in fat metabolism), lecithin, B-vitamins, and liver glandulars. Some dogs also get L-carnitine, especially if they have concurrent heart problems. We may use digestive enzymes such as lipase, to better utilize fat from the diet and body stores. We use fat soluble antioxidants such as vitamin E, and look at thyroid function. If necessary I set up a schedule for increased exercise (longer walks, swimming, etc.). Sometimes a previous injury prevents the animal from getting enough exercise, or enjoying the exercise it does receive. In those cases I try to help the animal repair and recover from those injuries.

Summary

All animals need fresh foods, including man. A variety of fruit, berries, melon, vegetables, seeds, monounsaturated fats, lean meats, and whole grains is the best insurance we have against disease. Pet food manufacturers do not have to disclose the sodium content of their foods. Poor water supplies, low magnesium content of commercial foods and high levels of salt can lead to sodium retention, hypertension and organ failure. Decreasing calories in the diet or adding high levels of indigestible fiber to prescription diets oversimplifies the process of weight reduction. We can help overweight dogs and cats by taking a more holistic approach to diet, exercise, lifestyle, and underlying medical problems.

4. Understanding cancer

A tumor or *neoplasm* is a mass of abnormal cells. There are three broad categories of tumors depending on the origin of the cells: carcinomas, sarcomas, and round cell tumors. A carcinoma is a tumor of epithelial cell origin. This group includes cancers of the skin, mucus membranes, and gland tissue (adenocarcinoma).

Sarcomas are tumors originating from mesenchymal or connective tissue. They include osteosarcoma (bone), leiomyosarcoma (smooth muscle), fibrosarcoma (fibrous connective tissue), and neurofibroma.

Round cell tumors are derived from blood cells, and include mast cell tumor, lymphoma, and myeloma (plasma cell tumor).

Cancer cells have unusual morphologic and growth characteristics that distinguish them from normal cells. Cancers are rapidly dividing, invasive clusters of cells that lack the differentiation and organization seen in mature cells. The carcinomas and round cell tumors have a tendency to metastasize or spread to distant sites. Cellular proliferation and growth in the absence of a continuing external stimulus defines *neoplasia*. Somehow the genetic regulatory mechanisms that govern cell division and maturation are gone in this event.

The phenomenon of *metastasis* occurs through separation of cancer cells from a primary tumor, and migration to distant sites via lymphatic or blood vessels, or across a body cavity. Metastatic disease is associated with a poor prognosis and failure of early therapeutic intervention.

A *benign* tumor has well-defined margins and the growth is entirely local. These tumors can still be locally invasive but do not metastasize. *Malignant* tumors have poorly defined

margins, and extend into surrounding tissues. They destroy surrounding tissue and ultimately lead to death.

Benign and malignant tumors may proliferate slowly or be rapidly dividing. A histologic examination of cell morphology, cell type, and tumor margins is needed to determine the growth characteristics of a tumor. The structure and function of a neoplasm varies from well differentiated, almost "normal" cells to poorly differentiated, totally aberrant cells that bear no resemblance to normal tissues.

How does cancer start in the body?

I try to rationalize the process of neoplasia to clients by stating that cancer starts from a toxic insult. It may be a sudden, overwhelming event such as exposure to a high dose of radiation, or chronic, low level exposure to tobacco smoke. In any event, the irritation to tissue is greater than our ability to repair the damage. The injury leads to a mutation in the genetic material of the cell or defect in cell regulation, causing uninhibited cell proliferation.

The key feature of carcinogenesis is a mutational event to genetic material, affecting the nuclear DNA or RNA. Mitochondrial DNA is also susceptible to mutations and aberrant gene expression. Any number of gene mutations, translocations, deletions, insertions, amplification of gene products, methylation of genetic material, and other changes could disregulate mitotic cell division and allow a tumor to grow. While DNA is the primary target of carcinogens, other macromolecules including repair enzymes and polymerases can be affected, causing mutations indirectly.

Tumor growth itself can be destructive to surrounding tissue, robbing adjacent cells of their blood supply, oxygen, and space. However some products of cancer cells can be harmful to the host, including hormone-like compounds, waste products, and enzymes. The effects of these products are included under the term, *paraneoplastic syndromes* and

may include neuropathy, dermatopathy, skeletal and connective tissue disorders, and mineral imbalances. See table below.

Tumor	Hormone produced	Clinical signs
Thyroid carcinoma, islet cell tumor, thymoma, oat cell tumor	Adrenocorticotropin (ACTH), Corticotropin releasing factor (CRF)	hyperadrenocorticolism, hyperglycemia, hypokalemia
Mast cell tumor	Histamine, kallikreins, serotonin	vasodilation, pruritis, diarrhea
Lung cancer	Anti-diuretic hormone (Vasopressin)	hyponatremia, hyperosmotic urine
Squamous cell carcinoma	Parathyroid hormone, prostaglandins, vitamin D-like steroids	hypercalcemia, hypophosphatemia
Sarcomas, liver cancer	Hypoglycemic factors	hypoglycemia
Liver cancer	Erythropoietin	ethrocytosis

Adapted from: Flax, MH, et al. Veterinary general pathology, 1994. Tufts University School of Veterinary Medicine, North Grafton, Massachusetts.

There are a couple of misconceptions about tumor growth worth mentioning here. First, individual tumor cells do not grow faster than normal cells. Tumors have a higher proportion of cells in a growth phase of the cell cycle, compared to healthy tissue. Chemotherapy is largely directed against cells that are in certain phases of mitosis.

Second, cancer cells are antigenic. Abnormal cells are recognized and destroyed by a functional immune system. Immunosuppressed individuals have a higher incidence of neoplasia than healthy individuals, and may be refractory to most cancer therapies. Without

normal regeneration of healthy tissue and a functional immune system, the cancer patient has little chance for survival.

Biopsy

A biopsy is the removal and microscopic examination of a sample of tissue. The purpose of a biopsy is to establish a diagnosis and grade the tumor. We commonly make use of fine needle aspirates, touch imprints, and excisional biopsies to make a diagnosis and guide our therapy. Needless to say, accurate tissue sampling and submission of the sample to a veterinary pathologist is essential for making an accurate diagnosis.

5. Metabolic Nutritional Analysis™

All of our cancer patients are on some form of nutritional therapy: either home prepared food, supplements, or both. Using standard blood and urine tests we formulate a nutritional plan for each patient. The standard blood tests we require are a comprehensive chemistry profile ("SuperChem" profile, Antech Diagnostic Laboratories, 1-800-872-1001) complete blood count (CBC), and thyroid profile (T_3, T_4, fT_4). The results of these tests are used to prepare a metabolic nutritional analysis (MNA) for the individual.

Metabolic Nutritional Analysis™ is a system of interpreting routine blood tests based on organ functional relationships. The purposes of the MNA are to identify:

1) **test results that deviate from the median value**
2) **subclinical nutritional deficiencies**
3) **organs that are under stress or diseased**
4) **nutritional therapy that addresses these imbalances**

Clients receive a five-page report and copies of the blood test results; this report and the telephone or office consultations to describe it comprise the MNA. Comparison of the latest serum chemistry profile with previous profiles helps us identify trends, such as progressive disease conditions. If our nutritional program worked, and owner compliance was good, we should see improvements in most if not all of the imbalances identified in the initial MNA.

Critical care patients are tested after two to four weeks of nutritional therapy. Most of our cases with a chronic, degenerative disease are tested after two to three months. Once the patient is stable or recovered we stretch the re-test interval to 6 - 12 months; shorter intervals for geriatric patients, longer for patients who are largely cured.

As with any diagnostic practice, these blood test results should be interpreted in context with the history, current medication(s), physical examination, and other aspects of the patient's health.

The MNA system includes certain organ functional relationships that are not apparent to many veterinarians. For example, one of the most common metabolic nutritional imbalances we see in dogs is relatively high serum sodium (>150 mEq/L). The conventional practice of regulating sodium balance is to either: a) add salt to food, b) feed a sodium-restricted diet, or c) select appropriate fluid therapy. That's what we're trained to do.

Sodium

Sodium balance is regulated at several points: in the salivary glands and gastrointestinal tract, the heart, chemoreceptors, adrenal glands, and kidneys. We do not intervene at all of these metabolic sites, but do recognize a wider interrelationship between sodium, the adrenal glands, other minerals, the heart, and kidneys.

Sodium balance is regulated by a number of hormones including mineralocorticoids from the adrenal cortex, e.g., aldosterone; atrial naturetic peptide from the heart, the renin-angiotensin system, transmembrane ion pumps in the intestinal brush border and renal tubules, and mass action with other ions.

An abnormal serum sodium value is an indication for nutritional support of the adrenal glands which probably play the central role in sodium homeostasis. Other indications for adrenal support include Addison's disease (hypoadrenocorticism), chronic inflammation, and chronic fatigue.

High levels of sodium in man are associated with hypertension and secondary cardiovascular, renal, and retinal disease. An acute rise in blood pressure of 30-50 mm Hg can cause a two- to threefold increase in urinary sodium output. Dogs apparently have a very efficient system of sodium conservation, and do not require the quantity of salt found in

commercial foods. Commercial pet foods may contain too much salt (sodium chloride) and too little potassium and magnesium for optimum health. Approximately half the canine patients in our practice have serum magnesium < 1. 7 mEq/L.

Knowing the connection between sodium and aldosterone, our interpretation of abnormally high or low serum sodium levels is to support adrenal gland function so that an appropriate hormone response will correct the imbalance. Aldosterone is probably more important for regulating potassium excretion and therefore the effect on sodium is indirect. By supporting the adrenal glands we also optimize the output of catecholamines from the adrenal medulla, and all of the cortisol-family of hormones that act in concert to regulate blood pressure.

Thyroid hormone also has a role in sodium homeostasis by enhancing Na-K-ATPase ion transport. Since the MNA includes thyroid testing, we are able to address all the organ functions involved in sodium balance: kidneys, adrenals, heart, thyroid, as well as diet and drug therapy.

Elevated liver enzyme activity including ALT, GGTP, and abnormal blood urea nitrogen values (normal creatinine) are indications for liver support. Similarly a low albumin level is an indication for nutritional support of the liver.

Gland therapy

In prescribing nutritional therapy to a patient we commonly make use of gland extracts or "glandulars". These are freeze-dried commercial products made from raw ovine, porcine, or bovine organs. Glandulars are available in a number of formulations including vanilla-flavored extracts, alcohol extracts, tablets, and capsules. There are single and multi-gland products, with or without additional vitamins and minerals. All are human food-grade nutritional supplements, though we find the quality differs among manufacturers. The daily dose for glandulars ranges from 1/3 tablet for a cat to 2 gland tablets for a giant breed dog. High quality glandular products cost less than 10 cents per tablet or capsule. Since

these products are virtually identical to the organ "meats" a wild carnivore would eat, their inclusion into a nutritional program couldn't be more natural. Freeze-drying the raw product helps to ensure freshness, stability in storage, potency, and therapeutic effect. They are the next best thing to eating fresh prey! Glandulars are inexpensive, safe, and effective therapy for supporting normal organ function in cats and dogs. Practically every patient in our practice that has an MNA receives some form of glandular therapy.

Thyroid function

Perhaps no other metabolic disease nicely illustrates the merits of nutritional medicine more than thyroid dysfunction. Hypothyroidism may be due to a myriad of organ dysfunctions, blocked receptor sites, or enzyme deficiencies. Thyroid hormone insufficiency may be due to problems with:

* iodine deficiency or excess
* decreased thyroxine (T4) synthesis
* decreased thyroid stimulating hormone from the pituitary gland
* decreased thyroid releasing hormone secreted from nerve endings in the hypothalamus
* decrease in thyroid-binding globulin
* decreased perfusion to the thyroid gland
* interference with thyroid hormone binding by cortisol or glucocorticoid drugs
* production of anti-thyroid antibodies
* chronic sympathetic tone, suppressing release of TSH
* non-thyroidal illness including diabetes mellitus, uremia, liver disease, and hyperadrenocorticism
* goitrogens in commercial pet foods[1]

With new patients I look at three thyroid hormones: T3, T4, and freeT4. Each gives me a clue as to the thyroid activity in the patient: the synthesis of hormone by the thyroid gland (T4), its circulation in the blood (as free T4), and conversion into active hormone (T3) in the thyroid gland, liver, and kidneys.

T4 is converted to T3 by the activity of a deiodinase enzyme; this enzyme requires selenium. If T4 is within the reference range, and T3 is low, I don't have a patient with a thyroid gland disorder, I have a patient with selenium deficiency. [2,3,4]

The hormone freeT4 is transported by a carrier protein that requires zinc. If T4 is normal but freeT4 is low, I don't have a thyroid gland disorder— I have a zinc deficiency. Patients may have any combination of low T4, T3, or free T4 and have clinical or subclinical hypothyroidism, but the cause and treatment of each condition may be different.

Exercise stimulates thyroid gland secretion and increases tissue sensitivity to thyroid hormone.[5] Vitamins A, E, and zinc function together to manufacture thyroid hormone from tyrosine. Vitamins C, riboflavin (B2), niacin (B3), and pyridoxine (B6) are also necessary for normal thyroid function. Magnesium is important for converting vitamin B6 to an active form, pyridoxal-6'-phosphate.

Magnesium

Magnesium is a very important macromineral, but one largely overlooked in small animal nutrition. Its primary function is enzyme activation, and it is involved in hundreds of enzyme pathways. The tissues with the highest magnesium concentration are also the most metabolically active, i.e., brain, heart, liver, and kidney. In healthy individuals intracellular magnesium concentrations are high; only potassium reaches a higher concentration.

Fish, meat, and dairy products are relatively low in magnesium. The best dietary sources are green, leafy vegetables, because chlorophyll (a plant pigment) is a chelate of magne-

sium. Commercial dog and cat foods appear to be barely adequate in meeting the daily requirement for this mineral. In humans, low serum magnesium is associated with heart disease, arrhythmia, hypertension, kidney stones, cancer, irritability, fatigue, weakness, problems in nerve conduction, muscle cramps and loss of appetite.

Most of the body store of magnesium is in the tissues, not serum. A low serum level is suggestive of clinical deficiency, though a more sensitive assay is red cell magnesium concentration. Low magnesium occurs more often in patients with inflammatory bowel disease, chronic diarrhea, or poor diet. Diuretic therapy can increase urinary excretion of magnesium. Magnesium levels should be evaluated with serum calcium, potassium, and phosphorus. It usually takes two to six weeks of oral supplementation to correct a magnesium insufficiency.

Conditions that may benefit from magnesium supplementation include:

* asthma, and chronic obstructive pulmonary disease
* cardiac arrhythmia
* dilated cardiomyopathy
* congestive heart failure
* hypertension
* mitral valve prolapse
* diabetes mellitus
* hypoglycemia
* nephrolithiasis

Diagnostic tests

A complete, working knowledge of the MNA program is beyond the scope of this seminar. What is important for treating cancer is to recognize the value of serum chemistry, urinalyses, and other diagnostic tests as a "window" into the patient's metabolic and nutritional disorders. Second, the interpretation of these tests goes beyond the training we re-

ceived in veterinary school. Third, inexpensive and safe nutritional supplements can be used alone as medical therapy to correct metabolic imbalance in cats and dogs. We believe the client should have copies of all laboratory test results. Our policy is to provide every MNA client with copies of all blood test results as well as our interpretation of those tests. After a reasonable interval, we ask the client to repeat the blood work and MNA. If our therapy was successful, we will see objectively, a clear improvement in the blood test results. Everyone stays better informed, and more actively involved in the healing process.

Do MNA's really work?

The success of the MNA program stems from the consistent way it evaluates routine blood tests, then guides the clinician towards the proper nutritional therapy. In order to achieve normal physiologic function one has to correct all the imbalances simultaneously. The MNA is an excellent system to do that. We find that the most effective way to correct metabolic imbalances is through prescribed use of natural, nutritional therapies that support normal repair mechanisms and work synergistically to promote good health.

Veterinarians and physicians interested in today's "functional medicine" or what Ronald Hoffman, M.D. calls "intelligent medicine" see medical conditions as more than a set of immediate signs and symptoms, to be treated with a more-or-less standard protocol of drug therapy. In the futuristic model, disease prevention is emphasized, rather than cures for existing conditions; client education is more important; and all therapeutic modalities are considered. Ultimately it is successful, long term outcomes that are the goal. In the future, small animal patients will visit veterinarians more for their diagnostic expertise than merely as a dispensary for drugs and vaccines.

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6. Cancer therapy

Conventional cancer therapy relies on surgery, radiation, and chemotherapy to effect a cure or long term remission. Veterinarians interested in complementary therapies also use conventional treatment, but augment it with nutritional therapy and immune support.

Radiation therapy is one of the more controversial treatments for killing cancer, as well as the least accessible to pet owners. (Radiation treatment is generally unavailable through local veterinary hospitals). Radiant energy in the form of x-rays, gamma-rays, and electromagnetic waves (including ultraviolet light) carry sufficient energy to damage biologically important molecules. X-rays excite electrons in animal tissue, producing numerous ionizations and excited chemical states. The excited electrons can create or break stable, covalent bonds in ring and double-bond structures. Nucleic acids are particularly susceptible to damage by ultraviolet radiation.

Ion pairs generated by ionizing radiation are unstable and have a short half-life of perhaps 10^{-10} seconds. They can recombine and form covalent bonds, or degenerate into free radicals. To destroy a tumor through radiation therapy, high voltage x-rays are directed at the tumor. The radiation energy excites water molecules in the tissue, releasing unstable oxygen species called *free radicals*. Examples of oxygen radicals include superoxide, peroxide, and hydroxyl radical. These free radicals have a relatively long half-life (10^{-5} seconds) and damage cell membranes, cell contents, enzymes and other macromolecules in solution.

Radiation treatment is potentially mutagenic, carcinogenic, and requires expensive, sophisticated equipment. Massive doses of x-rays destroy cells instantly, including non-target (healthy) tissue adjacent to the tumor. The main difference between healthy and tumor tissue is the ability of healthy tissue to repair itself after radiation injury. Moist, well-oxygenated tissue is more susceptible to radiation-induced free radical injury than anoxic tissue, e.g., necrotic areas in a tumor. Rapidly dividing cells are more

radiosensitive than cells not undergoing mitosis, making it possible to use external beam radiation or radioactive implants to destroy a tumor. Stem cells in bone marrow are highly susceptible to radiation injury, leading to anemia and leukopenia.

Surgery

Surgical removal of solitary tumors can be curative, especially if the cancer is detected early, the tumor is well-encapsulated, and surgical margins include all the malignant cells. Unfortunately at the time of surgery there is no rapid and reliable way to tell if the tumor is local or has metastasized. The main disadvantages of surgery include anesthetic risks, disfiguring surgery, and loss of function. Successful outcomes largely depend on the experience and skill of the surgeon.

Cryosurgery has proven to be a safe, low cost procedure for debulking tumors of the skin, perineum, and oral cavity. Liquid nitrogen is infused into a tumor until it looks and feels frozen. The dead tissue may slough after a few days to weeks, or persist as fibrous scar tissue. Aggressive oral tumors often require two or three treatments as it is difficult to achieve complete margins. Oral tumors that have invaded bone are very difficult to destroy with liquid nitrogen alone.

Angiogenesis inhibitors

Tumors need a blood supply to survive. Part of the normal inflammatory process is the expansion of new vessels into an area of injury, a process called neovascularization or *angiogenesis*. The process starts with local enzymatic degeneration of endothelial basement membrane. Endothelial cells migrate from the area to start a feeder vessel. With proliferation and maturation of endothelial cells, a capillary is formed. Recruitment of fibroblasts and collagen synthesis completes the network of new vessels.

Endothelial growth factors are produced by activated macrophages, platelets, endothelial cells, and fibroblasts. Tumors may initiate angiogenesis by *de novo* synthesis of growth

factors and cytokines, inhibit antiangiogenesis regulatory mechanisms, or incite enough local inflammation and tissue destruction to cause new vessels to form.

Recent work by Dr. Judah Folkman and others have isolated two promising compounds that control the proliferation of new blood vessels. Folkman has acheived a high degree of tumor regression in mice using these compounds that he calls "angiostatin" and "endostatin". Initially extracted from mouse urine, these compounds may someday be synthesized and made available to cancer patients.[1,2,3]

At present, we employ either shark cartilage or inositol hexaphosphate as natural angiogenesis inhibitors.[26] Cartilage has a relatively poor blood supply, and presumably blocks new vessel formation to tumors. Bovine cartilage is thought to have similar properties but is regarded as less effective than the shark products. Recent studies appear to validate some of the claims made for shark cartilage as an anticancer treatment.[24,25] Other natural sources of antiangiogenesis compounds include inositiol-hexaphosphate (phytic acid), [4-19] and soy fractions.[20,21,22,23]

Inostitol-hexaphosphate or IP-6 appears to have a *cytostatic* effect, serving as a regulatory molecule in cell maturation and apoptosis. I have started to use IP-6 against a variety of sarcomas and carcinomas as an angiogenesis inhibitor and tumor static agent. It has the potential to be a less expensive, more digestible, and renewable replacement for shark cartilage. IP-6 is commercially derived from brown rice bran but is also found in many whole grains. One source is: "Cellular Forte with IP-6", available from PhytoPharmica, 1-800-553-2370.

Ozone

Cancer cells will die in the absence of oxygen, or from lack of blood supply. Cancer cells can also be destroyed with high oxygen concentration, specifically those unstable oxygen species we call "free radicals". Ozone therapy has been used to treat cancer and other chronic diseases for over 50 years. Ozone or O_3 is used to purify municipal water systems

throughout Europe, much as we use chlorine to disinfect water. Chlorine in the presence of certain organic compounds can produce carcinogens such as trihalomethanes, whereas ozone water treatment is also germicidal but leaves no toxic byproducts.

Ozone can be administered to cancer patients as an intravenous infusion, intramuscular injection, enema, or intralesional injection. In human patients, a small volume (50 to 100 ml) of blood is drawn through an IV catheter, mixed with a small dose of ozone and infused back into the patient. A single treatment provides brief oxygenation to tissues for a few minutes to hours. Patients with gastric carcinoma can have their drinking water treated with ozone. Presumably the diseased tissue is more susceptible to free radical injury than healthy tissue (Healthy tissue would have normal stores and synthesis of antioxidant compounds).

Ozone may act upon the unique metabolic machinery of tumor cells or simply destroy cells that are susceptible due to inactive repair mechanisms. A 1980 report published in *Science* discussed ozone treatment of human tumor cells grown in culture. The cells were exposed to an ozone concentration of 0.8 ppm in air. Growth of tumor cells of lung, breast, uterus, and endometrium cancer was inhibited by 90 percent over the controls. The optimum dose of ozone is not well known, as too much ozone can damage healthy cells and may inhibit immune cells.

Ozone is not a discriminatory therapy; it attacks nucleic acids, intracellular and extracellular proteins, and lipid membranes. Successful administration of ozone gas is still more art than science, especially when the exact distribution or extent of cancer is unknown. Conventional practitioners may be comfortable using x-rays to generate oxygen radicals *in situ*, thus destroying the tumor. However a less expensive, safe and simpler treatment is to supply oxygen radicals in the form of O_3 directly into a tumor. Ozone generators can be purchased for less than $2000 and treatments administered on an outpatient basis. I have used intralesional ozone to treat a variety of mesenchymal tumors and found it to be a safe and effective therapy.

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7. Immune function

Cancer is a failure of immune surveillance and repair. At Smith Ridge Veterinary Center, the emphasis in cancer therapy is not on "killing cancer" but on supporting the immune system. Human patients that are immune deficient are 100 times more likely to die from cancer than the rate expected among immune competent individuals.[1]

The main disadvantage of conventional chemotherapy, radiotherapy, and surgery is the harm inflicted both to the body and the tumor. In contrast, the immune supportive measures we employ are not harmful to healthy tissue; they act only on diseased, damaged, or abnormal cells.

The body's defense system against cancer can be summarized in five steps:

1) **Antigen from damaged tissue is recognized by circulating white cells.**
2) **Antigen is degraded by enzymes and free radicals produced by white cells.**
3) **Circulating antibodies attach to membrane surface receptors or molecules.**
4) **Macrophage and Natural Killer cells engulf or lyse antibody-antigen complexes.**
5) **Arachidonic acid released from damaged phospholipid cell membranes promotes further inflammation**

To stop cancer cells through host immune functions, all components of the immune system including recognition of antigens, non-specific defenses, humoral and cell-mediated responses, etc. must be effective. It appears that the single most important accessory to the immune response is our nutritional status. For example, phagocytosis (the process of engulfing debris) is reduced during periods of hypoglycemia and in people with hypothyroidism. Diabetics and those with hyperglycemia have impaired T- and B-lymphocyte function. Excessive intake of some dietary fats such as ethyl palmitate and methyl palmi-

tate (from palm oil) can decrease phagocytosis of foreign tissue. There is still much to learn about the connections between diet, disease prevention, and treatment of cancer.

Complement

Complement is involved in *chemotaxis* of leucocytes and *opsonization* of foreign matter. It consists of nine plasma proteins that circulate in inactive form until activated by tissue injury, endotoxin release, antigen-antibody complexes, or polysaccharides. Complement promotes lysis of abnormal or tumor cells by stimulating migration of monocytes (is chemotaxic), regulating antibody production, enhancing phagocytosis of antigen (opsonization), and releasing anaphylatoxin for increased vascular permeability and smooth muscle contraction. These complex immune proteins also increase leukocyte degranulation with release of intracellular enzymes and stimulate production of more white blood cells.

Cytokines

Cytokines are polypeptides secreted by monocytes and lymphocytes in response to interaction with a specific antigen, a non-specific antigen, or a non-specific stimulus, i.e., the presence of endotoxin, or other cytokines. These signal molecules regulate the magnitude of inflammatory or immune responses.[2] Cytokines include interferons, tumor necrosis factor, interleukins, transforming growth factors, and hematopoietic colony-stimulating factors. (See table below).

Cytokines and their effects on the immune system.

Cytokine	Source	Major effects
IL-1	Monocytes, macrophages	Production of pyrogens, IL-6 and Colony Stimulating Factor; induces sleep, anorexia, inflammation, activates lymphocytes
IL-2	T cells	Stimulates T cell and B cell growth and differentiation
IL-3	T cells	Mast cell and hematopoietic cell growth
IL-4	T cells	T cell and B cell growth, increased IgE and IgG production
IL-5	T cells	differentitiation of eosinophils, increases IgA, and B cell growth
IL-6	T cells, monocytes, fibroblasts	Production of pyrogens, induces growth of plasma cell tumor, enhances Ig production, up-regulates production of acute phase proteins by liver cells, hematopoietic cell growth, differentiation of cytotoxic T lymphocytes
IL-7	Bone marrow and thymus stromal cells	Proliferation of pre-B and -T cells
IL-8	monocytes, endothelial cells, alveolar macrophages, fibroblasts	Chemotaxic for neutrophils, T cell activation
Interferon IFN-α, -β, -γ	T cells, fibroblasts	Inhibits viral replication and tumor growth, increases NK cell activity, modulates antibody response, activates macrophage cells
Tumor necrosis factor TNF-α	Monocytes, macrophages (cachectin)	Induces IL-1, increases adhesion molecules on endothelial cells, production of pyrogen, induces granulocyte colony stimulating factor, cytotoxic effect
TNF-β	T cells	Cytotoxic

Cytokines and their effects on the immune system. (continued)

Cytokine	Source	Major effects
Colony-stimulating factor, CSF	T cells, monocytes, macrophages, fibroblasts, endothelial cells	Stimulates growth of red and white blood cells, activates macrophages, increases eosinophil and leukotriene production, increases monocyte tumoricidal activity
Transforming growth factor TGF-α	Solid tumors (carcinomas, sarcomas), monocytes	Angiogenesis, proliferation of keratinocytes, bone resorption, tumor growth
TGF-β	T cells, B cells, platelets, kidney, placenta, bone	Proliferation of fibroblasts, synthesis of collagen and fibronectin, inhibition of cytotoxic T cells, NK, LAK cells; inhibits T and B cell proliferation; enhances wound healing and angiogenesis

Adapted from: Berkow, R., Editor. The Merck Manual of Diagnosis and Therapy, Sixteenth edition. Merck Research Laboratories, Rahway, NJ. © 1992, pp.284-285.

Killer cells

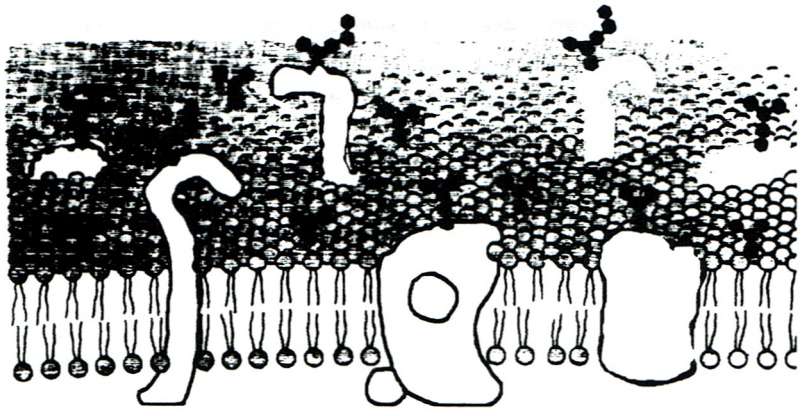
Natural Killer cells (NK) are subpopulations of lymphocytes that can kill cancer cells without prior sensitization. These non-specific, large, granular lymphocytes destroy neoplastic or viral infected cells by direct cytotoxicity. Basically they create channels in tumor cell membranes. Membrane damage to tumor cells by acid protein monomers called *perforins* is thought to occur in this way:

1) **T-cells recognize antigen present on the cell surface of tumor cells**

2) **T-cells bind to the cell membrane**

3) **Perforins stored in cytoplasmic granules, are ejected from the T-cell by exocytosis**

4) **Perforin protein monomers combine with calcium in the target cell membrane forming tube-shape polymers**



5) **Perforin polymers make pores through the cell membrane, causing a rapid influx of water and ions that burst the cell**

NK cells in man comprise 2 to 10 percent of normal peripheral blood lymphocytes. As outlined above, they lyse tumor cells after making direct contact and releasing perforin molecules that create holes in the tumor cell membrane. They do not require antibody, complement, or phagocytosis to kill the target cell. Other lymphocytes can be recruited to kill tumor cells under the influence of IL-2; these cells are called lymphocyte-activated killer (LAK) cells.

Prostaglandins

A variety of prostaglandins can be generated from arachidonic acid (from damaged cell membranes) by the action of phospholipases. They include PGE_2 which has a vasodilatory effect, increases vascular permeability and pain. $PGF_{2\alpha}$ causes smooth muscle contraction. PGI_2 or prostacyclin antagonizes thromboxane A2 and thus inhibits platelet aggregation and helps maintain renal perfusion. Prostaglandins are also released by neutrophils, mast cells, platelets, endothelial cells, and macrophages. They play a central role in modulating inflammation and can be partly manipulated by diet (essential fatty acid supplements) or drug therapy (steroidal and non-steroidal anti-inflammatory drugs).

Other means to regulate tumor cell growth include inhibiting *oncogenes* (tumor promoting genes) and switching "on" tumor suppressor genes. The mechanisms or molecular signals that regulate tumor cell replication are still under investigation.

Cell mediated immunity

The main features of cytotoxic, cell-mediated immune function can be summarized in the following way.

B lymphocytes produce antibodies

T lymphocytes secrete cytokines

✶ **Cytokines promote the proliferation, differentiation, and activation of B cells, T cells, macrophages, and other leucocytes.**

Natural Killer cells have anti-tumor cell activity.

Complement promotes identification and destruction of tumor cells and injured tissue through opsonization.

Antigen-presenting cells bind to tumor antigen. The macrophage cells release cytokines to activate T lymphocytes.

T helper cells react to the presented antigen and produce interferon-gamma and interleukin-2, which serve as growth factors for more macrophage and Natural Killer cells. T helper cells also stimulate proliferation and antibody secretion by B cells, and differentiation of suppressor T cells.

Antibodies provide anti-tumor specificity, optimizing the host's response.

It is critically important for the animal to control their immune response. Otherwise, there would be unlimited expansion of white cells, antibody production and depletion of immune resources. This self-control is carried out by suppressor T cells, macrophages, and regulatory cytokines.

Immune support implies that the patient receives nutritional and gland support for hematopoietic tissues including the bone marrow, liver, and spleen. Thymus glandular products and thymic proteins are indicated to support T-cell maturation. Lymph glandulars may be prescribed as well, to support clonal expansion and maturation of B lymphocytes. Finally, thyroid glandulars, thyroid extracts, or synthetic thyroid hormone are administered to cancer patients with documented low thyroid function. Thyroid hormones have an important role in activating leukocytes and upregulating hematopoiesis.

Immune surveillance

Tumors can "escape" or "hide" from the host immune system through several mechanisms.[3]

1) **Some tumor surface molecules may be poorly antigenic. The host may not respond to the tumor cells or be tolerant to them.**

2) **After binding with antibody, surface antigens may recede into the cell by endocytosis, escaping further immune surveillance.**

3) **Blocking antibodies may actually permit the tumor to grow, thus saving the liver from an overwhelming load of toxic products from tumor necrosis.**

4) **The tumor may be sequestered in a fibrous capsule, or coated with proteins (fibrin, sialomucin, etc.) that mask its surface.**

5) **Viral-infected tumor cells may be immunosuppressive.**

6) **Tumor cells may lack histocompatibility type I complexes, and go unrecognized by the host.**

Immunotherapy

Research has been directed at the application and production of natural immune-modulating substances to treat cancer. These include:

* Immune *adjuvants* such as mycobacterial cell wall fractions, mannins and other polysaccharides have been used to stimulate the number and/or activity of macrophage cells and lymphocytes.

* BCG (bacillus Calmette-Guérin) is a weakened (attenuated) tuberculin vaccine designed to stimulate macrophages. It has been used successfully to treat malignant melanoma and transitional cell carcinoma.

* Cytokines have been used experimentally to elicit a more favorable immune response against a tumor. These therapies have not been popular due to a number of adverse effects.

* Interferons have been used to activate macrophages and inhibit tumor cell division.

* TNF has direct antitumor activity. Problems in producing it in commercial quantities has limited its application in human patients.

* The pineal hormone *melatonin* has been used as a free radical scavenger and to amplify IL-2 in humans with metastatic tumor.[4] Melatonin has oncostatic properties[5] and is essential for normal adjustments to daylength. Melatonin has been effective at increasing hematopoiesis in patients with thrombocytopenia when the standard therapy was ineffective.[6]

* Injection of tumor antibodies from donors.

* Production of tumor-specific monoclonal antibodies through biotechnology.

At Smith Ridge Veterinary Center our efforts have been directed at nutritional support for the immune system and immune-stimulating natural therapies. Immunotherapy agents alone have not been satisfactory in bringing cancer patients into remission but may be part of a holistic treatment plan. I have used pineal glandular on many cancer patients (based on their Metabolic Nutritional Analysis™) and found it to be a useful adjunct in promoting restful sleep and enhancing the patient's well being.

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8. Immune Augmentative Therapy (IAT)

Immune augmentative therapy involves subcutaneous injections of processed serum that remove the effects of inhibitory proteins which protect the body from rapid tumor necrosis. Developed over twenty years ago, IAT is a safe and effective way to stop the progression of a tumor.

The main premise behind IAT is that a healthy immune system is capable of destroying cancer, but immune regulatory mechanisms interfere with the natural process. While many conventional cancer therapies act against the immune system, IAT therapy directs the immune response from inactive to an active state.

IAT supplements the body's auto-regulatory mechanisms to achieve a higher degree of tumor necrosis in patients with ineffective immune systems. The therapy is administered at home, by injecting minute quantities of serum to the cancer patient five days a week. Patients are tested every four weeks to evaluate their progress (tumor necrosis activity), and determine the next month's course of therapy. IAT serums are essentially non-toxic. They are derived from healthy donors as well as patients with cancer. This means the process of isolating and extracting serum components is relatively expensive.

Tumor necrosis

When a tumor is destroyed by chemotherapy, radiation, or an immune response, large quantities of cell wastes are released. Tumor necrosis can be toxic to the liver if the rate of destruction is too rapid or the quantity of wastes is more than the liver can detoxify. IAT recognizes this phenomenon and acts in a slow but gentle fashion. Many patients require months to a year of therapy in order to reach a remission from cancer.

The IAT program is based on the interaction of four components of tumor preservation or destruction:

* tumor blocking protein
* tumor deblocking protein
* tumor antibody
* tumor complement

Blocking protein has the temporary effect of protecting tumor cells from antibodies. Cancer patients who are immunosuppressed or immunodeficient are believed to have too much blocking protein, insufficient antibody, or both.

Deblocking protein neutralizes blocking protein and allows antibody to bind to the tumor. By administrating blocking protein or deblocking protein at appropriate times the immune response is directed at more tumor necrosis rather than less.

IAT does not claim to cure cancer. It restores immune competence in patients that have an inappropriate response to their disease. IAT has always been regarded as an adjunct to conventional cancer therapies, but can be used as primary treatment for many types of cancer.

The late Dr. Lawrence Burton, founder of IAT therapy, recognized that every individual has some aberrant or mutated cells that must be removed by the immune system even in health. He found healthy patients had tumor antibodies even though they did not have cancer. The next step was to identify the immune factors that contributed to cancer cell death, develop a test procedure to quantify them, and finally develop a process to isolate these factors and transfer them to cancer patients as therapy.

The beauty of Burton's approach is that it uses naturally occuring immune factors. While most cancer treatments are immune suppressive, IAT is not. It modifies a normal immune process that would protect the body from tumor necrosis, toxicity and overwhelming inflammation.

IAT Cancer Test

The IAT test is unique. It measures five serum components that are markers for tumor growth, death, and inflammation. These components are named: I1, I2, protein, tumor antibody, and tumor complement.

I1 I1 is a protein that appears 24 hours after tumor cells die. It is an indicator of tumor necrosis 24 hours prior to the time when the blood sample was obtained. The reference range for a healthy individual is 750 to 950.

I2 This protein is used to indicate tumor necrosis in the previous 5 days from the time the patient's blood was sampled. Like I1, the reference range for a healthy individual is 750 to 950.

Protein This is a measure of inflammation, but is not "total protein" as reported in routine serum chemistry tests. The reference range for a healthy dog or cat is approximately 1.25 to 1.30.

B1 B1 is tumor antibody. Every individual has some antibodies that can destroy cells that have undergone mutations or are abnormal. Reference range for a healthy patient is 0.60 to 0.65.

B2 Tumor complement. This is a peptide secreted by the tumor and gives us an estimate of tumor proliferation. As the tumor grows, more tumor complement appears in the circulation. Tumor complement is reduced in patients undergoing chemotherapy or receiving glucocorticoid drugs. Reference value for a healthy patient is 0.60 or less.

Patients are tested monthly. Serum proteins are identified by spectrophotometer and analyzed with a computer program. The results of the most recent test are entered into the computer program that generates a daily schedule of treatments, five days a week for the next four weeks. Patients usually receive three or four subcutaneous injections every 45 to 60 minutes, twice daily, with the weekend "off". It's an intensive effort and not every pet owner has the time or inclination to administer the injections. Some dogs and cats are poor candidates because they do not tolerate restraint or the injections. In the end, it is the pet

owner who is responsible for curing cancer or improving the quality of life of the cancer patient.

IAT administration

Small doses of IAT serum, typically 0.15-0.40 cc are injected through a 27-gauge x 5/8-inch needle or an insulin syringe. Clients have to keep track of six to eight different syringes each day, five days a week. A more "relaxed" schedule is optional, and we have clients who give morning-only treatment, or treat three days a week. The clinical outcome may not be attained as rapidly as the full five-day a week schedule, but is more manageable for some clients. In every case the dosage and frequency of each serum injection is based on the patient's progress rather than standard dose-response curves as would be applied to a drug.

IAT serum

The IAT serum proteins used for therapy are isolated from human or companion animal blood samples and extracted through a patented process at the IAT center in the Bahamas.[1] The serums are named: A2 A3, I, II.

A2 Deblocking protein. This is probably an alpha 2 macroglobulin, used to neutralize blocking protein so tumor antibodies can destroy a tumor in a tolerable way. The source is serum from a healthy donor. Levels of deblocking protein are significantly reduced in patients receiving radiation therapy.

A3 Blocking protein. This serum component prevents antibody binding to tumor cells and rapid tumor necrosis. The source is a blood clot from a healthy donor.

I Tumor antibody. Every individual has some antibodies to destroy cells that undergo mutations or are abnormal. Tumor antibody is probably derived from the IgG class.

II This is a one-third dilution of serum number I, tumor antibody.

How does IAT work?

We're not exactly sure how IAT evokes an immune response and causes tumors to stop growing or die. Briefly, pooled tumor antibody from numerous healthy donors is administered to the cancer patient. Tumor complement derived from blood clots of different patients with different forms of cancer activates tumor antibodies. The blocking and deblocking proteins are administered by injection at appropriate times and dosage to obtain a high degree of tumor necrosis. The logic behind the treatment schedule is buried in a computer program developed by the IAT group in the Bahamas. The program seems to work well for our patients. IAT serums are stored and shipped frozen. They contain no additives or preservatives, just a small amount of sodium potassium buffers. Clients thaw serum once, fill a four-week supply of syringes, and re-freeze. Each day's treatment (syringes of serum) are removed from the freezer and thawed before use. The main obstacle to acceptance of IAT by medical professionals is the lack of documentation and statistical analysis to support claims about its efficacy.

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9. Oxidative stress

Many chronic, degenerative diseases are associated with elevated levels of unstable oxygen species called "free radicals". The level of free radicals in tissues is associated with the extent of disease and effectiveness of our medical treatment.[1]

Free radicals are captured by free radical *scavengers* including antioxidant enzymes, vitamins, minerals, and a variety of plant compounds. Herbal and food sources of antioxidant compounds include quercetin (from blue-green algae, squash, and zucchini), anthocyanidins (from red, blue or purple fruits), pau d'arco (Brazilian tree bark), methyl-sulfonyl methane, beta carotene (from yellow and orange vegetables), and pycnogenol (French Maritime pine bark). The incredible diversity of beneficial antioxidant compounds from food plants, herbs, and algae has yet to be fully uncovered with modern analytical methods.

Antioxidant flavonoids from green tea, red wine, grape seeds, and other "medicinal foods" have been shown to have a variety of favorable effects on health including antibacterial, anti-inflammatory, antiallergic, antimutagenic, antiviral, antineoplastic, anti-thrombotic and vasodilatory activity.[2,3] In addition, different antioxidant compounds have affinity for different tissues and will localize in certain organs. For example, silymarin, the active principal from the herb milk thistle acts on the liver to increase glutathione synthesis up to 30 percent. Bilberry acts as a free radical scavenger inside the eye. Ascorbic acid from fruits and vegetables diffuses to virtually all tissues in the body, scavenging free radicals, and is eventually cleared intact by the kidneys, thus protecting the lower urinary tract from free radical injury. Hawthorne appears to be protective to heart muscle, and is commonly used in our practice to treat dilated cardiomyopathy, arrhythmia renal failure, and complications of diabetes mellitus.

Typical inflammatory changes seen under conditions of oxidative stress include the appearance of vacuolated macrophages or "foam cells"; increased cholesterol plaque in the circulation; erythrocyte rouleaux formation; deactivation of neutrophils; lipid membrane peroxidation; depolymerization of hyaluronic acid, and degradation of collagen and extracellular matrix.

Free radicals decrease alpha1-antitrypsin inhibitor, causing oxidative activation of the enzyme, *sialidase*. Sialidase in turn promotes the formation of fibrinogen, with potential adverse effects, especially in hypercoagulable states. Increased activity of sialidase has been shown to increase the destruction of polysaccharides and glycoproteins, serum proteins, and erythrocyte membrane surface proteins. Sialidase (also known as neuraminidase) cleaves sialic acid from the terminal ends of polysaccharides, depleting the high molecular weight compound. Polysaccharides are important substrate for numerous enzyme pathways and membrane receptors. This loss of a key substrate is thought to be a prelude to chronic, degenerative changes in the cell and tissues. The scientific literature is full of evidence to support the hypothesis that oxidative stress leads to degenerative disease. More attention is being given to the role of nutritional therapies to reduce the impact of free radicals and thereby prevent disease.

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10. Nutritional therapy

Nutritional therapy is used to enhance the immune system, reduce adverse local and systemic affects of cancer, and block or inhibit the growth of the tumor. Nutritional therapies include detoxification, immune support, enhancement of organ function, tissue repair, and improving mental health.

Cancer patients have to process large amounts of internal and external toxins. Internal toxins include metabolic wastes, tumor necrosis products, and opportunistic pathogens. External toxins include chemotherapy agents, analgesic drugs, flea and heartworm medications.

The main indication or benefit of nutritional therapy is prevention of cancer. Many studies show a positive effect from consuming a diet of fresh fruits and vegetables, monounsaturated vegetable oils, and whole grains. Appropriate diets for our cancer patients include fresh lean meat, fish, poultry, eggs, and liver. We encourage owners to prepare their pet's meals at home using fresh, whole foods. Approximately one-third of the diet should be vegetables, and one-quarter of the diet consisting of complex carbohydrates such as white potato, sweet potato, oats, barley, or brown rice. Most cancer patients should avoid an excess of meat fat. When animal fat is heated, a number of carcinogens are formed such as methylcholanthrene and nitrosamines.

Specific nutritional therapy should be based on each patient's individual chemistry and metabolic imbalances. The Metabolic Nutritional Analysis program offers a consistent method for identifying nutrient imbalances and prescribing natural therapies.

Vitamin C

One example of the use of nutritional therapy against cancer is ascorbic acid, or vitamin C. When we consume a food or supplement that contains vitamin C we obtain one of the best anti-cancer nutrients. Vitamin C can be taken orally, is widely distributed in tissues, gets cleared by the kidneys, and is eliminated still as vitamin C, in the urine. This versatile nutrient is found in all kinds of fruits and vegetables, but is sorely lacking in commercial pet foods. The prevailing assumption is that small animals synthesize adequate levels of vitamin C in the liver and do not require supplemental C in their diet.

Cats and dogs have the ability to synthesize small amounts of vitamin C from amino acids, but the amount produced *de novo* is nowhere near the amount of vitamin C that a wild cat (or dog) would obtain in their diet. While dogs and cats could survive without supplemental vitamin C, they can not maintain good health. Wild animals obtain substantial amounts of vitamin C every time they ingest the stomach and intestines of their prey, filled with partly fermented plant material. Obviously it's a little difficult to catch fresh game for our pets every morning, but a return to feeding them some fresh vegetables would go a long way towards restoring their health.

Vitamin C has been shown to protect cells from many common carcinogens. It can also be used in high doses as intravenous therapy to kill cancer cells.[1] Ascorbic acid can prevent formation of nitrosamines and N-methyl-N-nitrosoguanidine in urine, compounds that have been linked to bladder cancer. Vitamin C inhibits hyaluronidase, an enzyme produced by tumor cells that promotes metastasis. Low levels of vitamin C are associated with a decreased number and activity of T cells. Vitamin C also reduces histamine, thereby influencing gastric acid secretion. Patients with chronic pain, allergies, and other risk factors for gastric hyperacidity may benefit from additional vitamin C.

Vitamins and chemotherapy

All the antioxidant vitamins are useful adjuncts to chemotherapy protocols. For example, a number of published studies have demonstrated the benefits of vitamins A, E, and C in

preventing drug-induced toxicity of adriamycin. Tolerance of healthy tissue to radiation therapy is enhanced by administering supplemental beta carotene and other retinoids, vitamin C, or vitamin K. Patients undergoing radiotherapy that were supplemented with antioxidants had a higher level of tumor necrosis than patients who did not receive the supplemental vitamins.[2] Similar effects have been observed with selenium and N-acetyl cysteine.[3] Oncologists that advise clients not to give their dog or cat nutritional supplements when receiving chemo or radiotherapy are misinformed of the benefits of nutritional supplements used concurrently with conventional treatments. In general, nutritional supplements protect healthy tissue and do not interfere with the tumor-killing effectiveness of conventional cancer therapy. In some cases, nutritional supplements have been shown to potentate the destruction of cancer cells.

Coenzyme Q10 is a lipid-soluble antioxidant found in all cells, with the highest concentrations in mitochondria-rich cells such as those of the myocardium. In a study with three breast cancer patients, K Lockwood and workers placed the subjects on a daily oral dose of 390mg coenzyme Q10 (ubiquinone) during a multi-year trial. According to the paper, "the numerous metastases in the liver of a 44-year-old patient disappeared, and no signs of metastases were found elsewhere. A 49-year-old patient revealed no signs of tumor in the pleural cavity after six months. A 75-year-old patient with carcinoma in one breast, after lumpectomy and 390 mg of CoQ10 showed no cancer in the tumor bed or metastases."[4] Further studies will likely show the benefits of *tocotrienols* (from palm oil) as antioxidants and inhibitors of tumor cell growth.

Essential fatty acids

Essential fatty acids (EFAs) have recieved more attention lately as therapy for inflammatory diseases including osteoarthritis, colitis, asthma and allergies. Dietary long-chain unsaturated fatty acids protect vessel walls by maintaining cell membrane fluidity and regulating membrane receptors.[5] The three fates of dietary EFAs are to: 1) be used as an energy source, 2) serve as substrate for prostaglandin synthesis, or 3) be incorporated into cell membranes and maintain their fluidity.[6]

In animal tumor models omega-3 FAs have been shown to reduce tumor development and metastasis.[7] They also decreased the length of time for wound healing and protected local tissue from radiation injury. Omega-6 FAs stimulated tumor development. Typical North American diets contain a much higher proportion of omega-6 FAs relative to the omega-3's. American diets in the mid-1800's are thought to have a ratio of omega-6 to omega-3 FAs of approximately 1:1. Today that ratio is closer to 15:1 in our diet. Nutritionists recommend supplemental omega-3 FAs, to decrease the dietary ratio of omega-6 to omega-3s from 15:1 to 5:1. Good sources of omega-3s include marine fish oils, flax, borage, or evening primrose oil. Oilseed from the plant *Salvia hispanica* may be an important source of omega -3 FAs in the future. All of these unsaturated fats are highly subject to rancidity. We advise clients to purchase them in small quantities, and use up when they are still fresh.

Nutritional support for cancer patients

* encourage the feeding of fresh, whole foods
* replace commercial, processed pet food with "human quality" foods
* provide plenty of fresh, pure water
* correct vitamin, mineral, nutrient, and essential fatty acid imbalances
* support organ function and repair with raw "glandular" supplements
* provide adequate amounts of soluble and insoluble fiber in the diet
* improve nutrient digestion and assimilation with digestive enzyme supplements
* monitor the patient's body weight, body condition, and hydration
* avoid persistent flea and heartworm products, especially in patients at low risk of exposure
* avoid "routine" vaccinations in adult dogs and cats; monitor antibody titers instead and vaccinate only when the animal needs a booster

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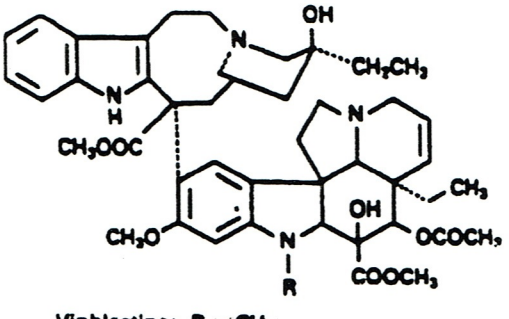
11. Phytomedicines

Herbs or medicinal plants are one of the oldest treatment modalities. Ancient Egyptians included a list of 700 herbal medicines in their historical record, Papyrus Ebers written around 1500 B.C. Today there are approximately 3000 medicinal herbs in use around the world, from rare and wild-gathered plants to large-scale fields of production. We could broaden our view of natural medicines to include pharmacologically active substances from bacteria, woody plants, fungi, insects and animals. Numerous examples of using natural medicines can be found in folklore but now the scientific basis for their use is being investigated.[1]

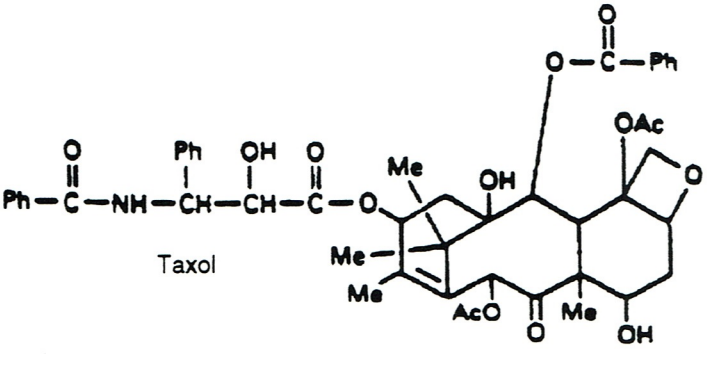
Chemotherapy agents

Some of the most common chemotherapy drugs are from plants. For example, vincristine sulfate and vinblastine are alkaloids that were isolated from the Madagascar periwinkle (*Vinca* spp.), a perennial herb. These alkaloids act by binding to tubulin, preventing mitosis.[2] Etoposide is a DNA-topoisomerase antagonist, and stimulates cleavage of DNA strands during replication. It is derived from the May apple, *Podophyllum peltatum.* The human cancer drug taxol (Bristol-Myers Squibb) is derived from the needles and bark of the Pacific yew, *Taxus baccata.* Its mode of action is to interfere with mitosis.



Vinblastine: R = CH_3
Vincristine: R = CHO

In general, the concentration of these pharmacologically active chemotherapy agents in the crude plant is too low to have much therapeutic value against cancer. The active compounds are extracted and concentrated, or synthesized to achieve a higher potency.



Taxol

Immune stimulating herbs

Echinacea is popular among people with colds and sore throats as an immune booster. This North American herb contains high molecular weight polysaccharides that have non-specific immune stimulating properties. *Echinacea* has been shown to enhance phagocytosis, and two of its compounds, a glycoside (echinacoside) and chicoric acid— may have antibacterial and antiviral properties.

Goldenseal (*Hydrastis canadensis*), is a North American herb that contains berberine and hydrastine, two alkaloids with antimicrobial properties. Goldenseal has been used to increase perfusion to the spleen, heal oral ulcers, and combined with deglycirrhyzinated licorice is one of the best remedies for gastric ulceration due to *Helicobacter pylori.*

The common spice cinnamon (*Cinnamomum cassia*) acts as an antipyretic, and stimulates blood flow. Cinnamon and ginger have been used for centuries to treat diarrhea, stomach cramps, nausea, and vomiting.

Herbs with a reputation for cleaning and toning the lymphatic system include cleavers (*Galium aparine*), echinacea, and poke root. Cleavers, also known as "goosegrass" contains coumarins, tannins, glycosides, and citric acid as active principals. The actions of this herb are diuretic and mild astringent. Cleavers is used to help the body eliminate toxins and to treat swollen or enlarged lymph glands.[4,5]

ESSIAC

Herbs can be used in combination to achieve a more potent medicinal effect, to reduce adverse effects of a primary herb, or to create synergistic effect. A popular herb combination for treating cancer is sold as a tea or tincture called "ESSIAC". Based on a traditional formula of an Ojibway medicine man, ESSIAC has been in use since the 1920's as a cancer remedy. ESSIAC was made popular by the late Rene Caisse of Ontario, who administered a combination of burdock root (*Arctium lappa*), turkish rhubarb root (*Rheum palmatum*), sheep sorrel (*Rumex acetosella*), slippery elm bark (*Ulmus rubra*), Watercress

(*Nasturt officinale*), kelp (*Laminaria digitata*), Blessed thistle (*Carduus benedictus*), and Red clover (*Trifolium pratense*) to her patients with cancer. Traditional healers relied on the root herbs to reduce tumor growth while the other herbs are said to help "purify the blood". (This means they support or enhance detoxification and clearance of waste products).

ESSIAC is believed to enhance immune function, improve metabolic detoxification, increase the patient's energy level or well being, and decrease inflammation.[6] This folk remedy has been used for a variety of different cancers, in part because it is safe, inexpensive, and readily available. "Original formula" ESSIAC tea and tinctures are readily available in health food stores or through mail order.

Burdock is one of the main herbs in the original formula. It contains benzaldehyde which appears to have antimutagenic and antitumor activity in humans.[7] The root contains up to 45 percent *inulin*, a polyfructosan or fructose oligosaccharide, as well as essential oils, vitamins and minerals. The Chinese consider burdock root to be a strengthening, tonic herb. Inulin is an interesting sugar that has been shown to have a favorable effect on postprandial hyperglycemia.[8]

Aloe emodin, catechin, and rhein in Indian rhubarb have shown antitumor activity in some animal tests. Aloe emodin has antileukemic activity. Rhubarb has been used for centuries for treating constipation. The roots are rich in iron but also contain anthraquinones, chrysophanol, physcion, sennidin, terarin, catechin, gallic acid, flavone, starch, pectin, and phytosterol. The active principals contribute to a dose-dependent laxative effect from this herb.

Slippery elm contains beta-sitosterol, a cholesterol antagonist and anti-inflammatory compound, and polysaccharides that are immune stimulating. The bark contains large amounts of tannins, mucilages, iodine, bromine, manganese, and bitter compounds. In Chinese medicine it is a *Yin* tonic; nutritive, demulcent, and expectorant. It is used in the most de-

bilitated patients or those with *chi* deficiency, regardless of age. Slippery elm lozenges or tea are soothing to sore throats, coughs, and dry airways. A gruel made with slippery elm will usually stay down when all other food causes nausea and vomiting.[9] Blessed thistle has been recognized since ancient times as a supportive treatment for the stomach and liver, in conditions of liver congestion, loss of appetite, hemorrhage, fever, or hepatitis. The aerial portions contain tannin, cnicine (a bitter compound), a sesquiterpeoid lactone, mucilage and traces of essential oil.[10]

Red clover blossoms are indicated in the treatment of all types of cancer. They contain isoflavones, coumarin, resins, vitamins and minerals. The coumarins have anti-coagulant properties and may be beneficial in hypercoagulable states such as myelomas.

The Chinese herbs, *ginseng* and *astragulus* have been in use for centuries for their immune stimulating properties. Considering the cost of new drug development, these traditional medicines offer a vast pharmacopea of safe and inexpensive adjunctive therapies. Herbs may act to suppress tumor cell growth, inhibit the transformation of non-carcinogenic compounds into carcinogens, block hormone receptor sites and thereby inhibit stimulation of sensitive tissues, up-regulate liver detoxification pathways, or scavenge free radicals. They often provide vitamins and minerals to nourish the patient while fighting cancer. The role of herbs and certain foods in preventing cancer is becoming more evident as we discover the compounds that can block carcinogens from their target sites. See table below.

Source	Cancer-protective compound
Broccoli, cabbage, kale, Brussel sprouts, watercress	isothyiocyanates (sulforaphane, indole-3-carbinol), glucosinolates*
Onion, garlic	organic sulfur compounds
Turmeric	curcumin
Citrus peel	monoterpenes
Numerous plants	flavonoids

Adapted from: Percival M. *Clinical Nutrition Insights* 1997 Jan;5(2):1-4

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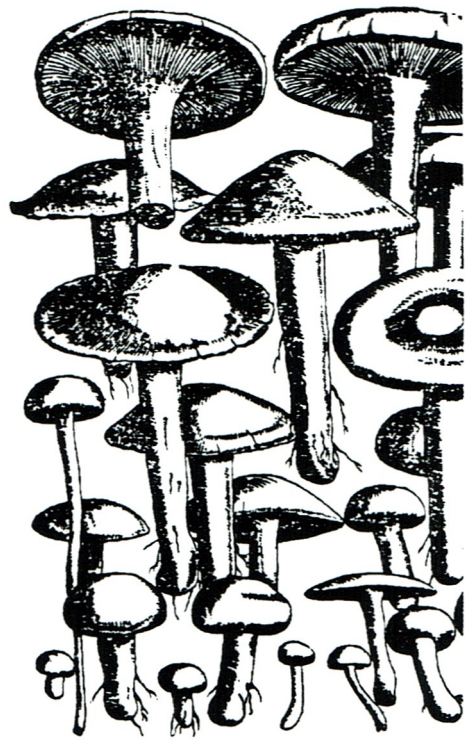
12. Medicinal fungi



Soil fungi, molds, yeasts, and bacteria are a source of some of the most common pharmaceuticals used in veterinary medicine. Drugs derived from molds, fungi, and bacteria include at least one class of anthelmintics, the *avermectins*; the antibiotics *penicillin* and *streptomycin*; and antineoplastic drugs such as *bleomycin*. It is not surprising that many species of medicinal fungi or "mushrooms" have been part of traditional medicine around the world. Recent scientific evidence supports the use of medicinal fungi for their immune enhancing and anti-tumor effects.

Among the 10,000 known species of fungi (and many more that have yet to be identified), a few stand out for their potent medicinal effect. Despite the mushroom's reputation as poison, the species used in traditional medicine have very low toxicity, and are considered to be nutritional supplements rather than drugs. The common constituent of these fungi are polysaccharides— long-chain, high molecular weight sugars such as *beta-glucan*. These polysaccharides appear to have antiviral, anti-tumor and immune stimulating properties. Other compounds such as triterpenes function as steroids in animals, with cholesterol-lowering or anti-inflamatory effects.[1]

The species used in our practice include Reishi (*Ganoderma lucidum*), Maitake (*Grifola frondosa*), Shiitake (*Lentinula edodes*), and Cordyceps (*Cordyceps sinensis*). They are combined with herbs in some of the traditional Chinese medicines we use.

Polysaccharides in Reishi have been shown to increase production of tumor necrosis factor (TNF) more than twenty-fold over controls, as well as increase the release of IL-1 and IL-6.[2,3]

Maitake mushroom contains 10 to 50 percent beta glucans on a dry weight basis. These branch-chain sugars are water soluble, but break into sub-fractions under heat, with a reduction in biological activity. 1,3-beta D-glucan stimulates cytokine production and TNF in macrophage cells. The complex sugars also have a moderating effect on blood glucose. Recent work supports the anti-tumor effect of Maitake which mediates cytokine release and stimulates the activity of lymphocytes and macrophages.[4,5,6] In a non-randomized clinical study of 165 advanced stage (III-IV) cancer patients, tumor regression or significant symptom improvements were observed in 11/15 breast-cancer patients, 12/18 lung-cancer patients and 7/15 liver-cancer patients treated with Maitake extracts. If Maitake were taken in addition to chemotherapy these response rates improved by 12-28 percent.[7]

Shiitake is the best studied and most popular medicinal mushroom.[1] It is even available as an injection for cancer therapy in Asia. The mushrooms are employed as tonic medicines for a variety of heart, asthma, infectious and neoplastic diseases. Active constituents in Shiitake include:

* Lentinan- beta D-glucan compound (M.W. 500,000)
* Heteroglucan
* Eritadenine- shown to reduce cholesterol
* Alpha-Mannan peptide
* Glycoproteins
* RNA - antiviral nucleic acids
* Hemicellulose- a cell wall carbohydrate
* Ergosterol- provitamin D

Similar compounds are found in the other species of medicinal mushrooms. *Cordyceps* however, is a bit more unusual. This species of fungi is a parasite of caterpillars rather

than a saprophyte of moist woody materials. Cordyceps deserves mention as a treatment for lymphoma, breast and lung cancer. It contains the polysaccharides galactomannin and mannose.

Mannin sugars such as acemannin are also found in the medicinal plant *Aloe vera*, and have anti-inflammatory properties. "Acemannan Immunostimulant" is an injectable pharmaceutical licensed for veterinary use. It consists of beta-(1,4)-linked mannan polymers interspersed with O-acetyl groups. The reconstituted solution is administered by intralesional and intraperitoneal injection to stimulate macrophage activity. The source for Acemannin immunostimulant is Carrington Laboratories, Inc. 1300 E. Rochelle Blvd., Irving, TX 75062. (1-800-255-4223)

For further information

The International Journal of Medicinal Mushrooms
Begell House, Inc., Publishers
79 Madison Avenue, New York, New York 10016
212-725-1999/Fax212-213-8386

MycoMedicinals®: An informational Booklet on Medicinal Mushrooms, by Paul Stamets. P.O. Box 7634, Olympia, WA 98507. © 1998. ISBN: 0-9637971-9-0

Medicinal Mushrooms: An exploration of tradition, healing and culture. By Christopher Hobbs, second edition.. Botanica Press, 10226 Empire Grade, Santa Cruz, CA 95060. ©1986, 1995.

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13. Antineoplastons

A common thread in many alternative cancer therapies is the belief that the body has all the mechanisms needed to rid itself of cancer. Dr. Stanislaw Burzynski has taken that concept to the next level by discovering endogenous compounds that have antineoplastic effects. His work has focused on low molecular weight compounds such as peptides and amino-acid derivatives.

Burzynski makes the distinction between cytokines, tumor necrosis factor, and immunoglobulins that characterize our immune response to cancer, from biochemicals and metabolites that alter gene expression and stop the proliferation of cancer cell lines in vitro. Burzynski named these molecules *antineoplastons* for their ability to inhibit cancer cell growth. His early work found that cancer patients were different from normal individuals in their concentration of certain compounds. For example, blood samples of advanced cancer patients had only 2 to 3 percent of the levels found in healthy individuals.[1]

One of the first antineoplastons isolated and put into therapeutic trials by Burzynski is phenylacetate. This simple compound is capable of suppressing *Ras* oncogenes that are responsible for malignant cell growth. Phenylacetate may also regulate the P53 tumor suppressor gene.

Antineoplaston therapy is offered to human patients through Burzynski's clinic in Texas. Patients receive injections and later, maintenance doses orally of specific peptides that bind to cancer cell DNA and transform the cell to normal gene expression, or promote transcription of genes that inhibit cancer cell growth. Another explanation for their mode of action may be the inhibition of protein synthesis in cancer cells.

Most antineoplastons prescribed for cancer therapy can be synthesized, but some are purified from human urine. These natural substances are well tolerated by the body, even in

high doses. Patients receive treatment for a minimum of four months, to one year. Burzynski has published his findings in more than 150 scientific papers and holds 20 patents on the antineoplaston treatment. His work has been confirmed by other research teams.[2-15]

Unfortunately the antineoplaston therapies that Dr. Burzynski administers are species-specific and are generally not effective in animals. Experience has shown that steady concentrations of antineoplastons must be maintained in the patient for the therapy to be effective, since these natural compounds are readily cleared from the body. Antineoplaston therapy is compatible with chemotherapy, radiotherapy, surgery, and immunotherapies. In some patients it has increased red and white blood cell counts by stimulating the bone marrow. Best results to date have been in the treatment of brain tumors, lymphomas, prostate, breast, and bladder cancer.

For further information:

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6221 Corporate Drive
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Tel. (713) 777-8233

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14. Detoxification

Medical science is finding more ways to identify our biological *individuality*. With the use of comprehensive digestive stool analysis, provocative liver function assays, and sensitive measures of urine excretory products we can now identify a patient's ability to assimilate and metabolize foods, neutralize toxins, and clear drugs out of their system. Understanding a patient's unique threshold for a specific medication will allow us to prescribe treatments with greater accuracy and safety, for the least cost.

Until last year, I avoided the term "detox" because I did not understand its origin or application. I realize now that detoxification is essential to health; indeed, we cannot live without removing waste through the elimination organs: the lungs, skin, liver, and kidneys.

Detoxification is defined as the process of changing a poisonous substance into a harmless one or removing it from the body so it will not cause harm. There are numerous detoxification pathways, including hundreds of cytochrome P-450 oxidase isoforms in the liver that have different affinities for the toxins we ingest or generate every day. Liver detoxification includes Phase I and II reactions that restructure undesirable compounds to facilitate their elimination in urine or bile. Basically this means transforming nonpolar, lipid-soluble molecules to polar, water-soluble molecules that are more easily excreted.

Though the liver is perhaps the most notable site for detoxification, the process takes place in all tissues and inside every cell. Inside the cell, the endoplasmic reticulum provides an extensive matrix and large surface area for detoxification to occur. Enzymes within the walls of the reticulum catalyze the breakdown of many substances. Through hydrolysis, oxidation, conjugation, acetylation, dehalogenation, and sulfonation scores of xenobiotics (toxic substances from food), drugs, and poisons are rendered harmless and readily excreted.

Cytochrome P-450 isoforms and detoxification of some common drugs.

Cytochrome	Target compounds
2E1	Imipramine
2C19	Halothane
2C9	Diazepam, ibuprofen, piroxicam
2D6	Phenytoin
3A4/3A5	Amitryptyline, cyclosporine,midazolam, lidocaine, erythromycin, ketoconazole, testosterone, estradiol, cortisol

Adapted from: Great Smokies Laboratory. Detoxification profile application guide. Feb 1997, p.2

Sulfation or sulfate conjugation is used to detoxify neurotransmitters, steroids, phenolic compounds, and drugs such as acetaminophen. The availability of sulfur may be rate limiting to this process. Patients with depressed clearance of steroid hormones may benefit from the addition of sulfur-rich foods to their diet, such as garlic, broccoli, or supplements of sulfur amino acids such as cysteine. It is interesting to note that veterinarians treat acetaminophen toxicity with N-acetyl cysteine (Mucomyst) but may not have made the connection between the antidote and detoxification pathways.

Detox is also a therapy; a way to promote liver and kidney function so harmful substances do not accumulate. Individuals with a genetic or acquired predisposition of impaired detoxification are very susceptible to adverse drug reactions and overdose. Detoxification therapy is aimed at providing proper substrate (nutrients) for enzyme synthesis and activity. This may include vitamins, antioxidants, minerals, animal or plant products that enhance the transformation and excretion of toxic metabolites or poisons.

Patients with gastrointestinal disease are good candidates for detoxification therapy. Intestinal injury by parasites, virus, bacteria, or the ulcerogenic effects of non-steroidal anti-inflammatory drugs dramatically increase the permeability of the intestines. Once the mucosal defense system is breached, an influx of inflammatory macromolecules, endotoxin, or xenobiotics can enter the circulation and assault the liver. The worst combination is to have a leaky gut and sick liver, as the toxic load can overwhelm the immune system.

In the future, veterinarians will use tests to identify individuals with weak detoxification mechanisms, and those tests will become more specific for common drugs. Supporting liver function will also help to remove excess steroid hormones.

Detoxification and cancer

Poor detoxification is an important consideration in the cancer patient. For example, women who smoke have a lower capacity to acetylate toxins from cigarette smoke, therefore are more at risk of forming carcinogens from tobacco smoke than normal women. The same individuals have a higher risk of developing bladder cancer. A complete detox program may involve diet modification to reduce the animal's body fat which is a storehouse of lipid-soluble toxins. In general, an effort should be made to improve liver function before a drastic weight-reduction program, or the rapid mobilization of toxins may overwhelm an already compromised patient.

Pathological detoxifiers can be identified as individuals with chronic liver dysfunction, multiple allergies, a history of adverse drug or vaccine reactions, and slow recoveries from anesthesia. Clearly, these patients have special requirements. They should not receive "aggressive" drug therapy! Instead, consideration should be given to homeopathic treatment for its low cost, safety, depth and breadth of the remedies.[1,2]

The detoxification process

Remove: harmful food additives, heartworm and flea products.

Restore: normal gastrointestinal function with beneficial bacteria, fiber and nutrients

Support: liver and kidney function with vitamins, minerals, pure water, and synergistic nutrients

I often recommend a one-week liver detox for patients with a history of poor diet, obesity, and chronic drug use. Many substances have been identified that induce P-450 enzymes: i.e., acetate from bacterial fermentation; niacin; riboflavin; sassafras; the brassica vegetables; oranges; and steroid hormones. Magnesium, iron, and molybdenum are P-450 cofactors. Substances that inhibit P-450 enzymes include cimetidine, erythromycin, hydrogenated fats, sugar, ketoconazole, heavy metals, and endotoxin. Deficiencies that impair liver function include those of B-vitamins, essential fatty acids, and thyroid; adrenal exhaustion, decreased perfusion, and cirrhosis.

Who needs detoxification?

Based on the history and physical exam findings, the patients that need detox may present with one or more of these conditions:

- ☐ lethargic, often fatigued
- ☐ lives with a smoker
- ☐ mentally dull, unable to concentrate
- ☐ constipated, has bowel movements less frequently than once a day
- ☐ obese
- ☐ has yeast infections (ear, skin, vagina)
- ☐ lives near a source of air or water pollution
- ☐ appears to have chronic pain
- ☐ has a history of food intolerance, or skin disease
- ☐ lacks fresh food in the diet
- ☐ history of chronic sinusitis
- ☐ gaseous distension, or malodorous stool
- ☐ on chronic drug therapy
- ☐ poor household water supply

Conditions where detoxification is contraindicated include pregnancy, animals that are hypothyroid, cachexic, or anemic. These patients need a higher plane of nutrition and uninterrupted clinical improvement.

Build on the initial progress made with detoxification by counseling pet owners on appropriate nutrition; the need for sunlight, exercise, fresh foods and clean water. Exercise boosts metabolic rate, oxygenation of tissues, circulation, and removal of metabolic wastes. Grooming and massage can be therapeutic as well, stimulating peripheral circulation and drainage of lymphatic vessels.

There are many herbs that can assist the patient in detoxification, such as echinacea, ginger, and red clover— the blood purifying, tonic herbs. Herbs with bitter principals such as Oregon grape root or burdock root are also good for clearing the liver of toxins, but I find most clients have better access to bitter leafy green foods from the supermarket.

One-week GI Detox

1. Feed 1 heaping Tablespoon of finely chopped bitter leafy greens for each 20 pounds of body weight twice a day for 7 days. Good choices are watercress, parsley, chicory, escarole, dandelion leaf, beet or mustard greens.

2. Feed 1 teaspoon of extra virgin, raw olive oil for each 20 pounds of body weight, twice a day, for 7 days. Olive oil supplies essential fatty acids and is a bile *secretagogue* and *cholegogue*. Bile flow helps eliminate xenobiotics (toxic, non-nutrients) that have been conjugated by the liver.

3. Feed one capsule of beneficial bacteria such as *Lactobacillus acidophilus* for each 20 pounds of body weight for one week.

These foods are to be administered in addition to the pet's usual diet. If I suspect chronic food intolerance, or inflammatory bowel disease (e.g., a history of foul smelling stool or soft diarrhea) I may include a supplement that binds endotoxin such as Ex-Tox (Nu-Biologics, Inc. 30W100 Butterfield Road, Warrenville, IL 60555-1512. Telephone 1-800-332-3130) containing vitamin C, DL-methionine, L-lysine, chlorophyll, bentonite, fruit pectin, garlic, and sodium alginate. Dose is one capsule for every 20 pounds of body weight, twice a day for 7 days.

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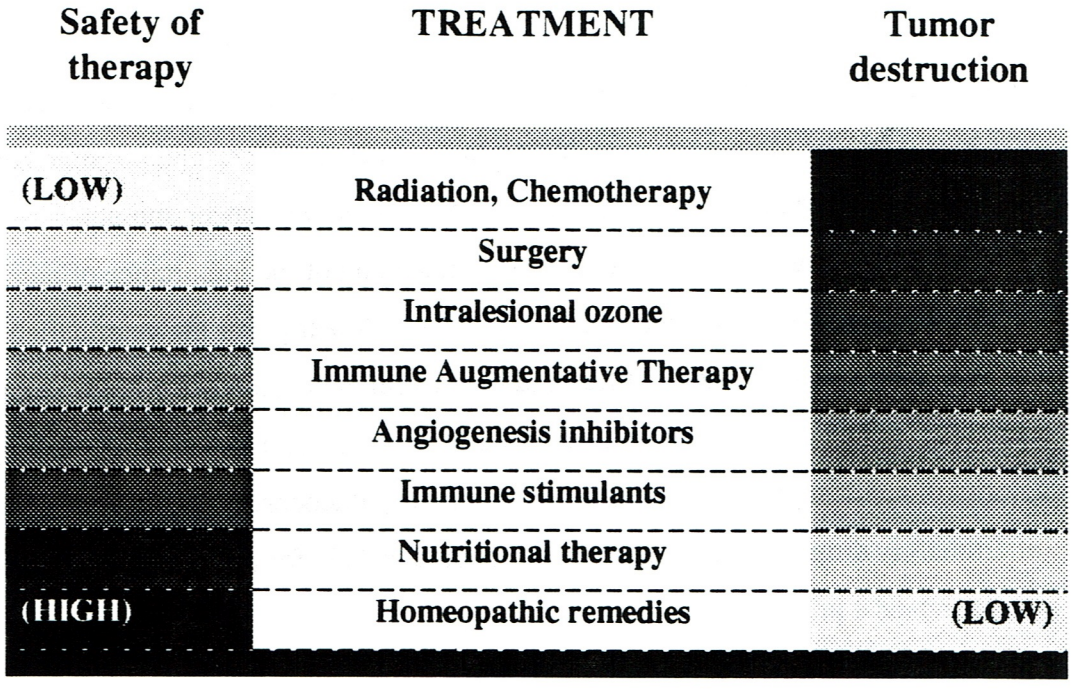
15. Conclusion

There is no single treatment that holds promise of a cure for cancer, but there are many ways to support the immune system, inhibit the growth of tumors, and promote healing. But first, clients need to be better informed about *preventing* cancer and other degenerative diseases. They need a better understanding of the importance of nutrition, exercise, and a healthy environment for their pet's well being. For the veterinarian, he or she needs to reassess the safety of flea and heartworm medications that disperse and accumulate in fatty tissues, our redundant use of vaccines, and chronic drug therapy. The majority of medications in veterinary use: antibiotics, glucocorticoids, non-steroidal anti-inflammatory drugs, and anti-histamines— should be held for the time when disease is present, not as a precaution.

Practically all companion animals today need the benefits of fresh, raw vegetables. Artificial ingredients, synthetic preservatives and near total reliance on processed food should be discontinued in favor of a more natural type of diet. Cancer patients about to undergo surgery, radiation or chemotherapy especially need the benefit of good nutrition.

Each form of cancer therapy can be compared for its efficacy in controlling cancer and its adverse side effects (see table below). In my experience, chemotherapy and surgery are effective treatments for many types of cancer. They're just too aggressive when administered without supportive care. In contrast, the use of homeopathic remedies alone do not cure cancer. The homeopathic remedy however is consistently safe and affordable; it has been used successfully to ease the discomfort of human cancer patients. Other natural therapies have slightly more risk of adverse effects, but have more documentation to support their effect on the immune system. There is no single cure for cancer.



In this seminar we've examined some of the science and concepts of alternative cancer therapy. It is my hope that the lines between "conventional" and "alternative" will cease to exist, as veterinarians in the next century integrate both forms of practice to treat this challenging disease. I have found many of these natural therapies to be effective at treating cancer patients while having a minimum of adverse effects. The fundamental lesson I have learned in practice is that every patient and every client has unique needs. While I can not elaborate a program that will work for every one of your patients, I hope that these pieces of holistic medicine will serve your patients well.

William Konrad Kruesi, M.S., D.V.M.

William Konrad Kruesi, M.S., D.V.M.
August 30, 1998

About the speaker

William K. Kruesi, M.S., D.V.M. is associate veterinarian at Smith Ridge Veterinary Center, South Salem, New York. His special interests include the application of natural therapies in small animal medicine. Kruesi graduated with honors from Tufts University School of Veterinary Medicine. He holds a Bachelor of Science degree, *Summa cum laude* in Plant Science, and a Master of Science degree in Horticulture from Rutgers University. He has completed one year of post graduate education in Animal Science from Cornell University, and pursued continuing education courses in veterinary homeopathy, applied kinesiology and clinical nutrition, feline medicine and surgery, ultrasound imaging, gastroenterology, neurology, and cardiology.

Smith Ridge Veterinary Center is a multi-doctor private practice that emphasizes a holistic approach to animal health. The veterinarians at Smith Ridge offer several types of non-toxic cancer therapies, nutritional analyses, homeopathic remedies, glandular, vitamin, mineral, and herbal supplements.

William Konrad Kruesi's interest in complementary therapies is due largely to the example set by his father, Dr. Oscar Rogers Kruesi, M.D., F.A.C.P. Dr. Oscar Kruesi is Director of New Health Initiatives, a clinical research facility for integrative medicine. This outpatient clinic emphasizes preventive health care using nutritional, conventional and alternative therapies. Dr. Kruesi has been in private practice for 42 years. In addition to his medical practice he is Chairman of the Department of Natural Medicine and Associate Professor of Clinical Medicine at Capitol University of Integrative Medicine, Washington, D.C.